United States Court of Appeals for the Federal Circuit

UNIVERSITY OF STRATHCLYDE,
Appellant

v.

CLEAR-VU LIGHTING LLC,
Appellee

2020-2243

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. IPR2019-00431.

Decided: November 4, 2021

CHRISTOPHER BRANTLEY KELLY, Alston & Bird LLP, Atlanta, GA, argued for appellant. Also represented by JASON P. COOPER; KIRK T. BRADLEY, Charlotte, NC; NATALIE CHRISTINE CLAYTON, New York, NY.

BRIAN J. EMFINGER, Banner & Witcoff, Ltd., Chicago, IL, argued for appellee. Also represented by MATTHEW PAUL BECKER, BINAL J. PATEL.

Before REYNA, CLEVENGER, and STOLL, *Circuit Judges*.

STOLL, *Circuit Judge*.

University of Strathclyde appeals from a final written decision of the Patent Trial and Appeal Board holding claims 1–4 of U.S. Patent No. 9,839,706 unpatentable as obvious. Because neither the Board's finding that the prior art disclosed all claim limitations nor its finding of a reasonable expectation of success is supported by substantial evidence, we reverse the Board's obviousness determination.

BACKGROUND

I

Methicillin-resistant *Staphylococcus aureus* (MRSA), and other Gram-positive bacteria[1] that have developed resistance to antibiotics, are "known to cause health problems, particularly in the hospital environment." '706 patent col. 1 ll. 38–58. The specification of the '706 patent explains that effective methods of controlling transmission of and rising infection rates from antibiotic-resistant bacteria is "becoming one of the most significant problems within the healthcare industry." *Id.* at col. 1 ll. 30–33. This is due, in part, to the "availability of few effective sterili[z]ation methods for environmental decontamination" of air and surfaces. *Id.* at col. 1 ll. 26–30.

The specification discloses that photoinactivation is a method that has emerged for killing harmful bacteria like MRSA. Previous photoinactivation methods involved treating an infection by applying a photosensitizing agent and activating the photosensitizing agent using light

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[1] Gram-positive refers to the results of a "Gram" stain, which is a test for determining what type of cell wall structure a given bacterium has. Whether a bacterium is Gram-positive or -negative determines which antibiotics can be used in a treatment plan.

energy, e.g., visible light having a wavelength in the region of 450–850 nm. *Id.* at col. 1 l. 59–col. 2 l. 9. While this technique has been shown to damage or kill certain bacteria such that their ability to grow is reduced or eliminated altogether, it suffers from "the significant practical disadvantage that photosensiti[z]ing agents must be applied to the bacteria that are to be inactivated." *Id.* at col. 2 ll. 11–15.

Scientists at the University of Strathclyde, recognizing this practical disadvantage, developed a method for photoinactivating antibiotic-resistant bacteria like MRSA *without* using a photosensitizing agent. Through numerous experiments, the inventors found that "[e]xposing [certain] bacteria to blue light, or white light containing blue light" having a wavelength in the region of 400–500 nm, "stimulate[s] an inactivation process." *Id.* at col. 2 ll. 50–52, 63–64. Specifically, the inventors experimented with different filters that allowed certain wavelengths of light to reach the bacteria, finding that wavelengths in the 400–500 nm region "provide[d] a high rate of [MRSA] inactivation." *Id.* at col. 5 ll. 11–13. These experiments led the inventors to conclude that "visible-light exposure over the wavelength range 400–450 nm is the major inducing factor for Staphylococcal [e.g., MRSA] inactivation, with increased inactivation occurring over the range 400–420 nm and optimum inactivation occurring at 405 nm." *Id.* at col. 5 ll. 36–40. The inventors also discovered that exposing bacteria such as MRSA to 405 nm blue light required a lower dose of light energy for inactivation compared to exposing bacteria to a broader wavelength range. For example, the inventors reported that a light dose of 945 J/cm^2 was required to inactivate MRSA when it was exposed to a broad spectrum of visible light greater than 400 nm, whereas a light dose of only 45 J/cm^2 was required for the cultures exposed to only 405 nm blue light. *See id.* at col. 6 ll. 37–49.

Based on their discoveries, the inventors developed a method of disinfection, which they claimed in the '706 patent. Claim 1 is illustrative of the claims on appeal and recites:

> 1. A method for disinfecting air, contact surfaces or materials by inactivating one or more pathogenic Gram-positive bacteria in the air, on the contact surfaces or on the materials, said method comprising exposing the one or more pathogenic Gram-positive bacteria to visible light without using a photosensitizer, wherein the one or more pathogenic Gram-positive bacteria are selected from the group consisting of Methicillin-resistant *Staphylococcus aureus* (MRSA), Coagulase-Negative *Staphylococcus* (CONS), *Streptococcus, Enterococcus*, and *Clostridium* species, and wherein a portion of the visible light that inactivates the one or more pathogenic Gram-positive bacteria consists of wavelengths in the range 400-420 nm, and wherein the method is performed outside of the human body and the contact surfaces or the materials are non-living.

Id. at col. 7 l. 17–col. 8 l. 5.

II

The Board determined that claims 1 and 3 of the '706 patent would have been obvious over Ashkenazi[2] in view of Nitzan,[3] and that claims 2 and 4 would have been

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[2] Helena Ashkenazi et al., *Eradication of Propionibacterium acnes by its endogenic porphyrins after illumination with high intensity blue light*, 35 J. FEMS Immunology & Med. Microbiology 17, 17–24 (2003).

[3] Yeshayahu Nitzan et al., *ALA induced photodynamic effects on Gram positive and negative bacteria*,

obvious in further view of Jones.[4] Because Strathclyde's appeal is focused on the Board's findings regarding Ashkenazi and Nitzan, we discuss each of those references below.

A

Ashkenazi is an article that discusses photoeradication of *Propionibacterium acnes* (*P. acnes*), a Gram-positive bacterium that is the leading cause of acne. Ashkenazi at 17. "In the case of *P. acnes* or other bacterial cells that produce porphyrins," Ashkenazi hypothesized, "blue light may photoinactivate the intact bacterial cells." *Id.* at 21; *see also id.* at 18 ("It has also been shown that when illuminated with blue light, porphyrins damage the cells very efficiently."). Ashkenazi suggested that light-activated porphyrin molecules contribute to bacterial cell death through release of free radicals.

Ashkenazi provides a method for photosensitizing *P. acnes*, which naturally produces high amounts of porphyrins, using δ-aminolevulinic acid (ALA), a photosensitizer[5] that enhances porphyrin production inside cells (i.e., endogenous porphyrins). To study the effects of ALA on inactivation, *P. acnes* was grown on a reinforced clostridial agar media supplemented with ALA and an unsupplemented media (i.e., without ALA) was used as a control. It is undisputed that clostridial agar would have contained

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3 Photochemical & Photobiological Scis. 430, 430–35 (2004).

[4] U.S. Pat. App. Pub. No. 2005/00550070.

[5] The Board construed the term "photosensitizer" to mean "a substance that, when applied to a target substance, makes the target substance more sensitive to light." *Clear-Vu Lighting LLC v. Univ. of Strathclyde*, No. IPR2019-00431, 2020 WL 3848045, at *7 (P.T.A.B. July 8, 2020) (*Final Decision*). Neither party challenges the Board's construction on appeal.

the vitamin riboflavin which, like ALA, is a photosensitizer. Thus, both of Ashkenazi's methods involved growing *P. acnes* in the presence of a photosensitizer—either riboflavin alone or together with ALA.

The cultures grew for up to 96 hours and were illuminated with 407–420 nm blue light at various light doses either once after 24 hours of growth or at consecutive 24-hour intervals. Both the ALA and non-ALA *P. acnes* cultures that were exposed to multiple, consecutive illuminations showed a decrease in viability of several orders of magnitude compared to cultures illuminated only once, and "[t]he decrease in viability of the cultures grown with ALA and illuminated with blue light was far more significant than that of cultures grown without ALA." *Id.* at 20. Ashkenazi also observed that increasing the light dose, e.g., from 75 J/cm^2 to 100 J/cm^2, likewise resulted in decreased viability for both the ALA and non-ALA *P. acnes*. Noting that "[t]he increase in the amounts of porphyrins in *P. acnes* as a result of ALA induction was significantly above the natural production of this bacterium," Ashkenazi concluded from these experiments that "the greater the intracellular amount of the porphyrin the better are the eradication results." *Id.* at 22.

B

Nitzan's authors, two of whom co-authored the Ashkenazi article, continued studying the effects of ALA on Gram-positive bacteria, including MRSA; the results were published just over a year after Ashkenazi's. Part of Nitzan's study focused on how exogenous porphyrins—i.e., a culture media supplemented with porphyrins—would affect inactivation. To do so, four different categories of MRSA cultures were prepared for the various bacteria, two of which were exposed to ALA, and two of which were not. Nitzan at 433 (Tbl. 5). For all of the non-ALA MRSA cultures, only some of which were grown on a media supplemented with exogenous porphyrins, Nitzan reported a

1.0 survival fraction, meaning there was "no decrease in viability . . . after illumination" with 50 J/cm^2 of 407–420 nm blue light. *Id.* at 433.

III

Clear-Vu Lighting LLC petitioned for *inter partes* review of claims 1–4 of the '706 patent on four separate grounds: (1) claims 1 and 3 are anticipated by Nitzan; (2) claims 2 and 4 would have been obvious over Nitzan in view of Jones; (3) claims 1 and 3 would have been obvious over Ashkenazi in view of Nitzan; and (4) claims 2 and 4 would have been obvious over Ashkenazi in view of Nitzan and Jones. *Final Decision*, 2020 WL 3848045, at *1–2. The Board instituted review. *See id.*

In its final written decision, the Board determined that Clear-Vu failed to prove by a preponderance of the evidence that claims 1 and 3 were anticipated by Nitzan, and that claims 2 and 4 would have been obvious over Nitzan in view of Jones. *Id.* at *22. Specifically, the Board found that Clear-Vu failed to demonstrate "that a 1.0 survival fraction measured for Nitzan's non-ALA induced MRSA demonstrates 'inactivation,'" which the parties agreed means, in the context of the '706 patent, that the "bacteria are killed, or damaged so as to reduce or inhibit bacterial replication." *Id.* at *10, 16; *see also* '706 patent col. 2 ll. 44–46.

The Board, however, agreed with Clear-Vu that claims 1 and 3 would have been obvious over Ashkenazi in view of Nitzan, and that claims 2 and 4 would likewise have been obvious over Ashkenazi in view of Nitzan and Jones. *Final Decision*, 2020 WL 3848045, at *22. Specifically, it found "Ashkenazi and Nitzan teach or suggest all the limitations of claims 1 and 3," and that a person of ordinary skill in the art would have been motivated to combine these two references and "would have had a reasonable expectation of successfully doing so." *Id.* at *20.

Regarding the scope and content of the prior art, the Board concluded that the only dispute was whether the prior art taught exposing bacteria to light without using a photosensitizer, finding that the "*combined* teachings of Nitzan and Ashkenazi" disclosed this limitation. *Id.* at *12–13 (emphasis added). In doing so, the Board summarily dismissed Strathclyde's arguments that neither reference taught this limitation, reasoning that Strathclyde "focus[ed] on Ashkenazi individually," not the combined teachings of Ashkenazi and Nitzan. *Id.* at *13.

The Board then found that a person of ordinary skill would have had a reasonable expectation of "inactivating MRSA using 407–420 nm light without applying a photosensitizer based on the combined teachings of Ashkenazi and Nitzan." *Id.* at *16. Although neither Ashkenazi nor Nitzan achieved inactivation of any bacteria without using a photosensitizer and, as the Board found, Nitzan failed to achieve any inactivation when it exposed MRSA to 407–420 nm light without applying a photosensitizer, *id.* at *10, the Board nonetheless found that a skilled artisan would have reasonably expected "some" amount of inactivation because the claims "do not require any specific amount of inactivation," *id.* at *16, 18. In doing so, the Board relied largely on Ashkenazi's teachings that increasing the light doses, the number of illuminations, and the length of time the bacteria are cultured resulted in greater inactivation for both the ALA and non-ALA *P. acnes* to support its finding that a skilled artisan applying Ashkenazi's teachings would expect at least "some" inactivation for non-ALA MRSA. *Id.* at *18. The Board ultimately concluded that claims 1 and 3 were unpatentable as obvious over Ashkenazi and Nitzan. *Id.* at *20. Because Strathclyde did not substantively address Clear-Vu's arguments with respect to claims 2 and 4, instead relying on the same arguments it made with respect to claims 1 and 3, the Board determined that claims 2 and 4 were unpatentable as obvious

over Ashkenazi, Nitzan, and Jones for the same reasons as claims 1 and 3. *Id.* at *21.

Strathclyde appeals, and we have jurisdiction under 28 U.S.C. § 1295(a)(4)(A).

DISCUSSION

We review the Board's legal conclusions de novo and its factual findings for substantial evidence. *Pers. Web Techs. v. Apple, Inc.*, 848 F.3d 987, 991 (Fed. Cir. 2017). "The substantial evidence standard asks 'whether a reasonable fact finder could have arrived at the agency's decision,' and 'involves examination of the record as a whole, taking into account evidence that both justifies and detracts from an agency's decision.'" *OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1381–82 (Fed. Cir. 2019) (quoting *In re Gartside*, 203 F.3d 1305, 1312 (Fed. Cir. 2000)).

"Obviousness is a question of law based on underlying findings of fact." *OSI Pharms.*, 939 F.3d at 1382 (quoting *In re Kubin*, 561 F.3d 1351, 1355 (Fed. Cir. 2009)). An obviousness determination generally requires a finding that "all claimed limitations are disclosed in the prior art," *PAR Pharm., Inc. v. TWI Pharms., Inc.*, 773 F.3d 1186, 1194 (Fed. Cir. 2014); *cf. Koninklijke Philips N.V. v. Google LLC*, 948 F.3d 1330, 1337–38 (Fed. Cir. 2020) (explaining that the common knowledge of a skilled artisan can be used to supply a missing limitation in some circumstances), and "that a person of ordinary skill in the art would have been motivated to combine or modify the teachings in the prior art and would have had a reasonable expectation of success in doing so," *OSI Pharms.*, 939 F.3d at 1382 (quoting *Regents of Univ. of Cal. v. Broad Inst., Inc.*, 903 F.3d 1286, 1291 (Fed. Cir. 2018)). Whether the prior art discloses a claim limitation, whether a skilled artisan would have been motivated to modify or combine teachings in the prior art, and whether she would have had a reasonable expectation of success in doing so are questions of fact. *Tech.*

Consumer Prods., Inc. v. Lighting Sci. Grp. Corp., 955 F.3d 16, 22 (Fed. Cir. 2020); *OSI Pharm.*, 939 F.3d at 1382.

On appeal, Strathclyde challenges the Board's obviousness determination, arguing that the Board erred in finding that the combination of Ashkenazi and Nitzan teaches inactivating one or more Gram-positive bacteria without using a photosensitizer. It also asserts that the Board's finding of a reasonable expectation of success is not supported by substantial evidence. We address each issue in turn.

I

We begin by addressing the Board's erroneous finding that the prior art disclosed all claim limitations. Both parties appear to agree that most of the limitations found in claims 1 and 3 are disclosed by Ashkenazi or Nitzan; the only dispute is whether these references teach inactivating one of the claimed Gram-positive bacteria without using a photosensitizer. The Board's finding that this was taught by the combination of Ashkenazi and Nitzan is not supported by substantial evidence.

Claims 1 and 3 require both exposing the claimed Gram-positive bacteria to 400–420 nm blue light without using a photosensitizer *and* that the bacteria are inactivated as a result. While Ashkenazi discloses culturing *P. acnes* both with and without ALA such that it achieves inactivation after exposure to 407–420 nm blue light for (1) ALA *P. acnes* and (2) non-ALA *P. acnes*, the parties agree that the media Ashkenazi used to culture *P. acnes* contained the vitamin riboflavin, a photosensitizer. *See Final Decision*, 2020 WL 3848045, at *12; *see also* J.A. 2139–40 (Goodrich Decl. ¶ 121). It follows, then, that all of Ashkenazi's *P. acnes* cultures were grown in the presence of a photosensitizer—either riboflavin alone, or riboflavin together with ALA. We see nothing in Ashkenazi that discloses or suggests inactivating *P. acnes*, or any other bacteria, without using a photosensitizer.

In addition, although Nitzan provides an example in which MRSA and other bacteria were exposed to 407–420 nm blue light without ALA or any other photosensitizer, there is no evidence that Nitzan successfully achieved inactivation under this condition. Indeed, in finding that Nitzan did not anticipate claims 1 and 3, the Board found Clear-Vu failed to establish that Nitzan's non-ALA MRSA demonstrated "inactivation" as required by the claims. *See Final Decision*, 2020 WL 3848045, at *10.

In making its contrary finding that the combination of references disclosed this limitation, the Board credited Clear-Vu's argument that a skilled artisan would have prepared a MRSA culture according to the method described in Nitzan—which, unlike the media used to culture *P. acnes* in Ashkenazi's experiments, would not have contained riboflavin—and applied Ashkenazi's teaching that increasing the light energy, number of illuminations, and length of time the bacteria are cultured may result in greater inactivation for both ALA and non-ALA bacteria, as was shown for *P. acnes*. *Id.* at *13. The Board found that this combination, therefore, "disclose[d] exposing bacteria to light without using a photosensitizer." *Id.* Given neither Ashkenazi nor Nitzan teaches or suggests inactivation of *any* bacteria *without* using a photosensitizer, we fail to see why a skilled artisan would opt to entirely omit a photosensitizer when combining these references. Indeed, the Board articulated no rational basis[6]—and we discern

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[6] Although the Board relied on and found persuasive the testimony of Clear-Vu's expert, Dr. Sulzinski, discussing this modification to Nitzan's non-ALA MRSA, *see id.* at *13 (citing J.A. 2336 (Sulzinski Decl. ¶ 77)), the Board discredited testimony from this *same* paragraph in Dr. Sulzinski's declaration in its anticipation analysis because he "merely state[d] . . . his opinion, and offer[ed] no evidence" to support his statements, *id.* at *10 (citing J.A. 2336

none—for combining Ashkenazi's *P. acnes* experiments, which at all times used a photosensitizer, with Nitzan's non-ALA MRSA experiment, which did not achieve inactivation, to arrive at an embodiment in which MRSA is inactivated by exposing it to 407–420 nm blue light *without* using a photosensitizer. We find it particularly relevant that Nitzan itself disclosed such a photosensitizer-free embodiment and was wholly unsuccessful in achieving inactivation.

Nor are we persuaded that Ashkenazi and Nitzan, either individually or in combination, "disclose[] the particular 'inactivating' and 'inactivates' language" found in claims 1 and 3 as Clear-Vu suggests. Appellee's Br. 57. Importantly, the claims require that the inactivation is a result of exposing bacteria to 400–420 nm light *without using a photosensitizer*, which is neither taught nor suggested by the prior art of record. We decline Clear-Vu's invitation to read the inactivation limitation in isolation, divorced from the claim as a whole. *Cf. ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 546 (Fed. Cir. 1998) ("Obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention." (cleaned up)).

On this record, we conclude that no reasonable fact finder could have found that the combination of Ashkenazi and Nitzan discloses inactivating one or more Gram-positive bacteria without using a photosensitizer. The Board's finding to the contrary is not supported by substantial evidence.

II

We turn next to the Board's findings on reasonable expectation of success. The Board found that a skilled artisan

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(Sulzinski Decl. ¶ 77)). This inconsistency in the Board's credibility findings further undermines its findings here.

would have expected that MRSA could be inactivated by blue light without using a photosensitizer due to the presence of at least some amount of naturally produced porphyrin in the bacteria. We disagree. The only support for such a finding is pure conjecture coupled with hindsight reliance on the teachings in the '706 patent.

Starting with the references themselves, neither Ashkenazi nor Nitzan provides a skilled artisan with any evidence or data or other promising information showing successful inactivation of *P. acnes*, MRSA, or any other bacteria without using a photosensitizer. These references thus contain no suggestion that a skilled artisan would reasonably expect that MRSA or one of the other claimed Gram-positive bacteria could be inactivated upon exposure to 407–420 nm blue light *without* using a photosensitizer. The Board nevertheless found that a skilled artisan would have expected that MRSA could be inactivated by 407–420 nm blue light without using a photosensitizer because, as both parties agree, MRSA naturally produces "at least some" amount of endogenous porphyrins. *Final Decision*, 2020 WL 3848045, at *17. The Board, relying on Ashkenazi's teaching that "blue light *may*" inactivate "*other bacterial cells* that produce porphyrins," Ashkenazi at 21 (emphases added), reasoned that because light-activated porphyrin molecules were shown in Ashkenazi to cause inactivation for *P. acnes* (even though Ashkenazi's experiments applied a photosensitizer), the fact that MRSA has some level of endogenous porphyrin suggests to a skilled artisan that MRSA, too, would exhibit some amount of inactivation after exposure to 407–420 nm blue light. But there is simply no evidence of record at the time of the '706 patent to support this assumption. In fact, the evidence of record—Nitzan and an earlier publication

authored by Dr. Nitzan in 1999 (Nitzan 1999[7])—shows the opposite, illuminating the error in the Board's finding.

In the late 1990s, Dr. Nitzan and his colleagues "examined the effects of the accumulation of endogenous porphyrins on" MRSA. Nitzan 1999, Abstract; *see also id.* at 270 (explaining that the tested *S. aureus* strain was methicillin-resistant). As with the later studies described in Ashkenazi and Nitzan, Dr. Nitzan exposed both the ALA and non-ALA MRSA to doses of 400–450 nm blue light ranging from 0–50 J/cm^2. The survival fraction at each light dose for the non-ALA MRSA was 1.0, *id.* at 274 (Fig. 3(a)), meaning there was no decrease in viability and thus no inactivation, whereas the viability of the ALA MRSA decreased by "3–4 orders of magnitude," *id.* at 273. Dr. Nitzan reported the same results for the non-ALA MRSA only a couple of years later. *See* Nitzan at 433 & Tbl. 5 (reporting a 1.0 survival fraction for non-ALA MRSA after illumination with 50 J/cm^2 blue light, meaning "no decrease in viability").

Dr. Nitzan's experiments thus are directly contrary to the Board's rationale for why a skilled artisan would have expected success in inactivating MRSA in the absence of a photosensitizer. Even accepting as true that MRSA naturally has "at least some" amount of endogenous porphyrins, the data Dr. Nitzan reported would have indicated to a person of ordinary skill in the art that those natural levels are insufficient to inactivate MRSA using 407–420 nm blue light without also using a photosensitizer.

In finding that Clear-Vu had established a reasonable expectation of success, the Board dismissed the data reported in Nitzan and Nitzan 1999 because, in its view, it

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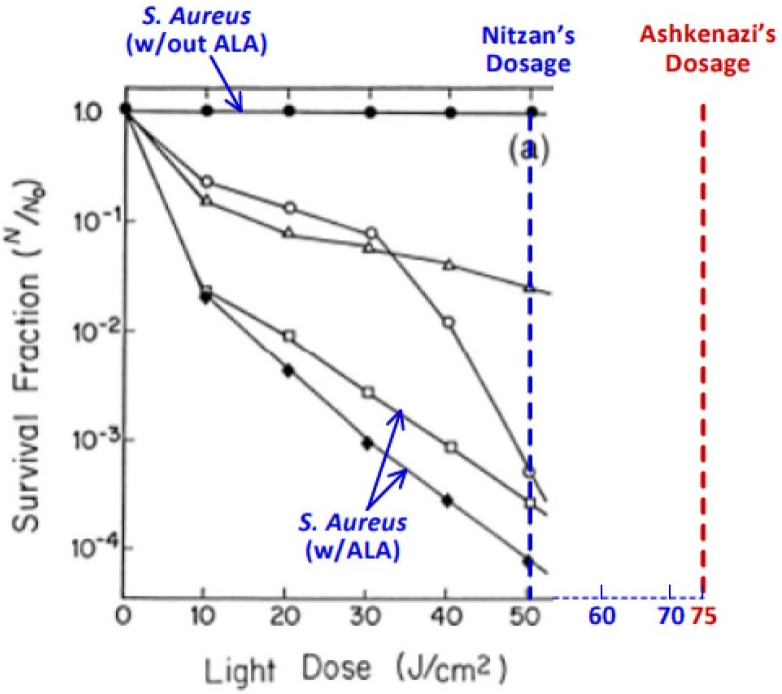
[7] Y. Nitzan & M. Kauffman, Endogenous Porphyrin Production in Bacteria by δ-Aminoleavulinic Acid and Subsequent Bacterial Photoeradication, 14 Lasers Med. Sci. 269 (1999).

would lead a skilled artisan to the "*limited conclusion* that non-ALA-treated MRSA incubated for 4 hours and treated with a single dose of 50 J/cm^2 light showed no decrease in activity." *Final Decision*, 2020 WL 3848045, at *18 (emphasis added); *id.* ("We reach a similar conclusion for the data reported in Nitzan 1999, which only shows data up to a light intensity of 50 J/cm^2, the same intensity used in Nitzan."). The Board based its finding largely on the fact that neither Nitzan nor Nitzan 1999 tested light doses above 50 J/cm^2, reasoning that using an increased light dose, such as the 75 J/cm^2 dose used in Ashkenazi's experiments, would cause inactivation of MRSA based on Ashkenazi's finding that increased light doses resulted in greater inactivation for both ALA and non-ALA *P. acnes*. *Id.* at *17–18.

The Board's reasoning finds no support in the record. The only evidence before the Board on this issue was the unrebutted testimony of Strathclyde's expert, Dr. Goodrich, who testified the opposite. *See* Oral Arg. at 12:22–15:05, http://oralarguments.cafc.uscourts.gov/default.aspx?fl=20-2243_05032021.mp3 (Clear-Vu conceding it did not provide rebuttal testimony on this point). Dr. Goodrich explained that a skilled artisan "viewing th[e] graphical representation of Nitzan 1999's data would have *clearly expected* the curve of the ALA-absent *S. aureus* [MRSA] data *to remain flat* as dosage increased to 75 J/cm^2," J.A. 2133 (Goodrich Decl. ¶ 107) (emphases added), as shown below in his annotated version of Nitzan 1999's Figure 3(a):



J.A. 2132–33 (Goodrich Decl. ¶ 106). Dr. Goodrich then concluded that, to a skilled artisan, "the data in Nitzan 1999 would have indicated that the response of MRSA without ALA to blue light at 75 J/cm^2 *would have been the same* as 50 J/cm^2—no bacteria would have been killed." J.A. 2133 (Goodrich Decl. ¶ 107) (emphasis added).

The Board gave no weight to Dr. Goodrich's testimony because, in its view, Dr. Goodrich did not provide the underlying facts forming the basis for his opinions. *See Final Decision*, 2020 WL 3848045, at *18 (citing 37 C.F.R. § 42.65(a)). We disagree. In his declaration, Dr. Goodrich specifically relied on and analyzed Nitzan 1999's data in forming his opinions. Given that the Board's stated reason for discrediting this written testimony is unsupported by the record before us, we see no reason to "defer[] to the special province of the Board to exercise its discretion concerning the credibility of expert witnesses" as Clear-Vu

suggests we do here. Appellee's Br. 49 (citing *Yorkey v. Diab*, 601 F.3d 1279, 1284 (Fed. Cir. 2010)).

Thus, not only is there a complete lack of evidence in the record that any bacteria were inactivated after exposure to 407–420 nm blue light without using a photosensitizer, there is also evidence showing that others had *failed* to inactivate MRSA—one of the claimed Gram-positive bacteria—without using a photosensitizer, despite experimenting with different light doses and different wavelength ranges of blue light. We have found that such failures undermine a finding of a reasonable expectation of success.

For example, in *OSI Pharmaceuticals*, we reversed the Board's obviousness determination because its finding of a reasonable expectation of success was not supported by substantial evidence. 939 F.3d at 1384–85. The claims at issue in *OSI* were directed to a method of treating non-small cell lung cancer (NSCLC) using a therapeutically effective amount of a drug known as erlotinib. *Id.* at 1378–79, 1384. The Board found that two different prior art combinations would have provided a skilled artisan with a reasonable expectation of success in using erlotinib to treat NSCLC in a mammal. *Id.* at 1384. We disagreed, explaining that none of these references contained "data or other promising information regarding erlotinib's efficacy in treating NSCLC." *Id.* at 1384; *see also id.* at 1385. We also found it significant that, during the time of the invention, there was a 99.5% failure rate for other drugs entering Phase II clinical trials that, like erlotinib, were targeted for the treatment of NSCLC. *Id.* at 1385. Thus, given the "failure rate" and lack of "data or any other reliable indicator of success," we found that "the only reasonable expectation at the time of the invention was failure, not success." *Id.*

Such is the case here. In view of Dr. Nitzan's reported failures for MRSA and lack of any "reliable indicator of success," we fail to see how Ashkenazi's prophetic statement

about what "may" happen when "other bacterial cells" are exposed to blue light would lead a skilled artisan to reasonably expect that MRSA could be inactivated when exposed to 407–420 nm blue light *without* using a photosensitizer. The Board's finding that a skilled artisan would expect at least "some" inactivation for non-ALA MRSA—in view of Ashkenazi's teaching that increasing the light doses, the number of illuminations, and the length of time the bacteria are cultured can result in greater inactivation based on experiments that were conducted using a photosensitizer—is not supported by substantial evidence.

In attempting to support the Board's findings, Clear-Vu argues that support can be found in the '706 patent itself. *See* Appellee's Br. 58 ("It *defies logic* to conclude that inactivating MRSA by applying Ashkenazi's technique to Nitzan's MRSA would not result in inactivating MRSA when the patentee obtained that very result using the same technique." (emphasis added)). But "[t]he inventor's own path itself never leads to a conclusion of obviousness; that is hindsight. What matters is the path that the person of ordinary skill in the art would have followed, as evidenced by the pertinent prior art." *Otsuka Pharm. Co., v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012). Given the record on appeal, as with *OSI*, we are left to conclude that "[i]t is only with the benefit of hindsight that a person of skill in the art would have had a reasonable expectation of success in view of the asserted references." *OSI Pharms.*, 939 F.3d at 1385.

Contrary to Clear-Vu's arguments, we do not hold that "absolute predictability" or "guaranteed success" is required to find a reasonable expectation of success. Appellee's Br. 43, 45 (emphasis omitted). To be sure, we have repeatedly rejected that notion. *See, e.g.*, *Acorda Therapeutics, Inc. v. Roxane Lab'ys, Inc.*, 903 F.3d 1310, 1333 (Fed. Cir. 2018) ("This court has long rejected a requirement of '[c]onclusive proof of efficacy' for obviousness." (alteration in original) (quoting *Hoffmann-La Roche Inc.*

v. Apotex Inc., 748 F.3d 1326, 1331 (Fed. Cir. 2014))); *OSI Pharms.*, 939 F.3d at 1385; *PAR Pharm.*, 773 F.3d at 1198. We reaffirm today that absolute predictability of success is not required, only a reasonable expectation. In this case, where the prior art evidences only failures to achieve that at which the inventors succeeded, no reasonable fact finder could find an expectation of success based on the teachings of that *same* prior art. The Board's finding is not supported by substantial evidence, and we therefore reverse its obviousness determination.

CONCLUSION

We have considered the parties' remaining arguments but find them unpersuasive. For the foregoing reasons, we reverse the Board's obviousness determination.

REVERSED